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(51) International Patent Classification ⁷ : C07B 39/00, C07J 9/00, C08F 8/22, C08J 7/12	A1	(11) International Publication Number: WO 00/68170 (43) International Publication Date: 16 November 2000 (16.11.00)
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(54) Title: FLUORINATION IN LIQUID OR SUPERCRITICAL CARBON DIOXIDE (57) Abstract A method of fluorinating a substance comprises providing a reaction mixture comprising a liquid or supercritical carbon dioxide reaction medium, a first reactant, and a second reactant, wherein the first reactant is a fluorinating reagent, and then contacting the first reactant and the second reactant in the carbon dioxide such that the first reactant fluorinates the second reactant.		

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FLUORINATION IN LIQUID OR SUPERCRITICAL CARBON DIOXIDE

Field of the Invention

The invention generally relates to processes for fluorinating compounds in carbon dioxide.

Background of the Invention

5 Fluorination, which is generally defined as the contacting of elemental fluorine, or another fluorinating agent, with a substance, is an important industrial process. The choice of fluorinating agent and fluorination conditions often determine the selectivity of the fluorination. The fluorinated substance generally undergoes a temporary or permanent change in its physical or
10 chemical properties. Among the changes typically observed in fluorinated substances are bleaching, purification, enhanced lubricity, enhanced impermeability to certain materials, reduction in flammability, and inertness toward chemical reactions such as, for example, resistance to oxidation. The specific changes that are seen, and their magnitude, often depend upon the
15 fluorination conditions as well as on the nature of the substance that is fluorinated. Fluorination can effect changes in the structure of molecules, for example, by replacing certain atoms or groups of atoms such as hydrogen, chlorine, bromine, iodine, carbonyl groups, and hydroxyl groups with fluorine. Fluorine may also be added to sites of unsaturation such as carbon-carbon
20 double bonds. Fluorinating agents that are often used include, but are not limited to, elemental fluorine, xenon difluoride, and functional amines (e.g., N,N-diethyl-1,1,2,3,3,3- hexafluoropropylamine.

Fluorination is typically carried out in solvents or media that are resistant to reaction with fluorinating agents such as halogen-containing

solvents like carbon tetrachloride, chlorofluorocarbons, and fluorocarbons. Notwithstanding any potential advantages, these solvents or media may pose potential health and environmental concerns, and should be controlled to minimize possible exposure of personnel and release to the environment.

- 5 Such environmental concerns could become problematic since selective fluorination processes are being explored for use in pharmaceutical research.

Thus, there is a need in the art for solvents for fluorination and processes using the same that do not have the shortcomings referred to above.

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Summary of the Invention

The present invention obviates the need for employing organic solvent reaction media in fluorination processes, particularly processes involving pharmaceutical compounds. In one aspect, the invention provides a method
15 of fluorinating a substance. The method comprises providing a reaction mixture comprising a liquid or supercritical carbon dioxide reaction medium, a first reactant, and a second reactant, wherein the first reactant is a fluorinating agent. The first reactant and the second reactant are then contacted in the carbon dioxide reaction medium such that the first reactant fluorinates the
20 second reactant.

In another aspect, the invention relates to a reaction mixture. The reaction mixture comprises a first reactant comprising fluorine, a second reactant; and a liquid or supercritical carbon dioxide reaction medium. The first reactant and the second reactant are present in the carbon dioxide
25 reaction medium and the first reactant and the second reactant react such that the second reactant becomes fluorinated.

A further discovery is that carbon dioxide may facilitate the fluorination of solid articles, so that fluorination may be faster and penetrate more deeply than is found when fluorine gas is used alone.

30 These and other aspects and advantages are provided by the present invention.

Brief Description of the Drawings

FIG. 1 is an SEM photograph of fluorinated high density polyethylene (HDPE) processed in accordance with a method of the invention; and

FIG. 2 is an SEM photograph of fluorinated low density polyethylene (LDPE) processed in accordance with a method of the invention.

Detailed Description of the Preferred Embodiments

The present invention now will be described more fully hereinafter with reference to the accompanying specification and examples, in which preferred
10 embodiments of the invention are shown. This invention may, however, be embodied in many different forms and should not be construed as limited to the embodiments set forth herein. Rather, these embodiments are provided so that this disclosure will be thorough and complete, and will fully convey the scope of the invention to those skilled in the art.

15 In one aspect, the invention relates to a method of fluorinating a substance. The method comprises providing a reaction mixture comprising a liquid or supercritical carbon dioxide reaction medium, a first reactant, and a second reactant. The first reactant comprises fluorine and, for the purposes of the invention, may be considered a fluorinating agent. The first reactant
20 and the second reactant then come into contact in the carbon dioxide such that said first reactant fluorinates the second reactant. In the invention, neither, either, or both of the first and second reactants being soluble in carbon dioxide.

Although not wishing to be bound by any theory, the second reactant
25 can be thought of as having "reactive sites" that allow for the second reactant to be fluorinated. More specifically, the term "reactive sites" is defined as a location on the second reactant that is capable of reacting with the first reactant (i.e., a fluorinating reagent). Any number of types of reactive sites in accordance with the above definition may be employed for the purposes of
30 the invention. For example, the second reactant may have a reactive site in the form of an unsaturated bond (e.g., a double or triple bond) which may react with the first reactant such that the fluorine becomes attached to the

second reactant. As an example, the fluorine may be covalently bonded to the second reactant.

The second reactant may have at least one active group or substituent. For the purposes of the invention, an "active group" is an atom, substituent, or the like, which is known to be capable of being replaced by fluorine in a fluorination reaction by virtue of the reaction between the first reactant and the second reactant. Examples of active groups include, but are not limited to, hydrogen, hydroxyl, carbonyl, and halogens (e.g., chlorine, bromine, or iodine). Examples of second reactants having hydroxyl groups include, but is not limited to, 1-octanol, 2-octanol, and cholesterol.

For the purposes of the invention, carbon dioxide is employed as a fluid in a reaction mixture in a liquid or supercritical phase. The reaction mixture typically employs carbon dioxide as a continuous phase, with the reaction mixture typically comprising from about 50 to about 99.5 percent by weight of carbon dioxide. If liquid CO₂ is used, the temperature employed during the process is preferably below 31°C. In one preferred embodiment, the CO₂ is utilized in a "supercritical" phase. As used herein, "supercritical" means that a fluid medium is at a temperature that is sufficiently high that it cannot be liquefied by pressure. The thermodynamic properties of CO₂ are reported in Hyatt, *J. Org. Chem.* **49**: 5097-5101 (1984); therein, it is stated that the critical temperature of CO₂ is about 31°C. In particular, the methods of the present invention may be carried out at a temperature range from about 0°C to about 110°C. The pressures employed typically range from about 800 psia (5.5 mPa) or to about 5000 psia (3.4 mPa).

As stated hereinabove, the first reactant that is employed in the method of the invention may be characterized as a fluorinating reagent. The term "fluorinating reagent" is defined as a material capable of fluorinating to another compound, such as, for example, a monomer, polymer, or other type of material. Examples of fluorinating agents include, but are not limited to, elemental fluorine, nucleophilic fluorinating agents (e.g., N, N-diethyl-1,1,2,3,3,3-hexafluoropropylamine), and electrophilic fluorinating agents (e.g., xenon difluoride, hypofluorites). Mixtures of any of the above may be employed. The fluorinating agents that are used are typically soluble in

carbon dioxide. The reaction mixture preferably comprises from about 0.5 to about 50 percent by weight of the first reactant or fluorinating agent.

The second reactant that is utilized is one that typically contains at least one reactive site as defined herein. Examples of second reactants
5 include, but are not limited to, organic compounds, organic polymers and inorganic polymers. Included in the above are pharmaceutical compounds. For the purposes of the invention, the term "pharmaceutical compound" is to be broadly construed to cover a wide range of pharmaceutically active compounds. Examples of pharmaceutical compounds include, but are not
10 limited to, sterols (e.g., cholesterol), carbohydrates, amino acids, peptides, nucleosides, antibiotics, anesthetics, mixtures thereof and other materials. Mono- and polyfunctional alcohols may also be employed and include, but are not limited to, cyclohexanol, benzyl alcohol, 1-octanol, 2-octanol, and the like.

Examples of organic polymers that may be fluorinated by the methods
15 of the invention encompass high density polyethylene (HDPE) and low density polyethylene (LDPE). As an example, the polymer may be in the form of an article such as a container, tank, pipe, bottle, plate, rod, or other shape. These articles are sometimes treated with fluorinating agents to fluorinate their surfaces. Fluorination improves chemical resistance, impermeability to
20 hydrocarbons and other liquids and gases, resistance to staining, among other benefits known to those skilled in the art. We have found that fluorination in a reaction medium of carbon dioxide in accordance with this invention can result in a deeper penetration of the fluorinated layer in solid polymer without an increase of contact time, or an equivalent penetration at a
25 shorter reaction time.

The polymers may be fluoropolymers, especially highly fluorinated polymers, that is polymers in which more than 90 percent of the monovalent atoms on the polymer are fluorine. The polymers may be perfluoropolymers. The polymers may be in forms suitable for melt processing. This includes
30 finely divided form such as powder, or it may be pellet or cube form, such as is used in injection molding or extrusion. In general, the polymer may be in the form of a shaped article. The shaped article may be, for example, a vessel having an interior surface which is exposed to said first reactant. It is

often necessary to treat fluoropolymers, and especially perfluoropolymers, with fluorine to fluorinate reactive end groups in order to improve the thermal stability of the polymers, particularly thermal stability during melt processing. The reactive end groups come from polymerization initiator radicals, or chain
5 transfer agents that are used in making the polymers. Fluorination of fluoropolymer powders, pellets, and cubes proceeds more rapidly and completely in the carbon dioxide reaction medium in accordance with this invention.

Various additives may be used in the reaction mixtures employed in the
10 methods of the invention if so desired. Examples of these additives include, but are not limited to, additives that regulate molecular weight of the fluorinated products or that control its functionality. Reagents that may control process variables such as reaction times, alter the flow characteristics of the fluid used for the reaction medium may also be employed. Optionally, co-
15 solvents may be used. Mixtures of any of the above components can be employed as known by one skilled in the art.

The methods of the invention may be carried out using known equipment. For example, the fluorination reactions may be carried out either batchwise, continuously, or semi-continuously, in appropriately designed
20 reaction vessels or cells. Additional features may be employed such as, for example, agitation devices (e.g., a paddle stirrer or impeller stirrer) and heaters (e.g., a heating furnace or heating rods).

The following examples are intended to illustrate the invention and are not intended as a limitation thereon. In general, the examples are provided to
25 demonstrate the effectiveness of the methods of the invention. Table 1 is presented and provides a general summary of each example.

Table 1

Example	Substrate	Fluorinating Agent	Condition	Temp (°C)	Pressure (psia)	CO ₂ Density	HF Scavenger	Product*
1	Saturated liquid hydrocarbon	Electrophilic	SC CO ₂	105	5000	0.69275	None	30
2	Saturated cyclic secondary liquid alcohol	Nucleophilic	Liquid CO ₂	25	1000	0.73939	None	0
3	Unsaturated liquid alcohol	Nucleophilic	Liquid CO ₂	25	1000	0.73939	None	60
4	Saturated acyclic primary liquid alcohol	Nucleophilic	Liquid CO ₂	25	1000	0.73939	None	68
5	Saturated acyclic secondary liquid alcohol	Nucleophilic	Liquid CO ₂	25	1000	0.73939	None	48
6	Saturated cyclic secondary solid alcohol	Nucleophilic	Liquid CO ₂	25	1000	0.73939	None	62
7	Saturated cyclic secondary solid alcohol	Nucleophilic	Liquid CO ₂	0	1000	0.95522	None	28
8	Saturated cyclic secondary solid alcohol	Nucleophilic	Liquid CO ₂	25	1000	0.73939	None	33
9	Saturated cyclic secondary solid alcohol	Nucleophilic	Liquid CO ₂	25	1000	0.73939	Sodium Fluoride	37
10	Saturated cyclic secondary solid alcohol	Nucleophilic	SC CO ₂	40	1200	0.31559	None	51
11	Saturated cyclic secondary solid alcohol	Nucleophilic	SC CO ₂	40	1500	0.65219	None	45
12	Saturated cyclic secondary solid alcohol	Nucleophilic	SC CO ₂	40	2000	0.76064	None	33
13	Saturated cyclic secondary solid alcohol	Nucleophilic	SC CO ₂	40	3000	0.84676	None	29
14	Saturated cyclic secondary solid alcohol	Nucleophilic	SC CO ₂	40	4500	0.91596	None	26
15	Hydrocarbon polymer (HDPE)	Fluorine gas	No CO ₂	21-23	16	-----	None	12-21
16	Hydrocarbon polymer (HDPE)	Fluorine gas	Liquid CO ₂	21-23	850	0.76343	None	54-62
17	Hydrocarbon polymer (HDPE)	Fluorine gas	SC CO ₂	34-35	1150	0.49399	None	65-75
18	Hydrocarbon polymer (HDPE)	Fluorine gas	No CO ₂	34-35	16	-----	None	29-42
19	Hydrocarbon polymer (LDPE)	Fluorine gas	No CO ₂	34-35	16	-----	None	12-20
20	Hydrocarbon polymer (LDPE)	Fluorine gas	No CO ₂	21-23	16	-----	None	19-20
21	Hydrocarbon polymer (LDPE)	Fluorine gas	Liquid CO ₂	21-23	850	0.76343	None	42-58
22	Hydrocarbon polymer (LDPE)	Fluorine gas	SC CO ₂	34-35	1150	0.49399	None	42-65

Example 1

A 25 mL high pressure reactor equipped with a pressure transducer and temperature controller was purged with dry nitrogen for approximately 15 minutes. The reactor was charged with carbon dioxide and 2.0 mL methylcyclohexane and 0.5 g of xenon difluoride. The whole reaction system was closed and the reaction mixture was stirred at 105°C and at 5000±15 psi (3.4 ± 0.1 mPa) for 3 hours. The resultant solution mixture was analyzed by ¹H NMR and GC/MS.

Example 2

A 25 mL high pressure reactor equipped with a pressure transducer and temperature controller was purged by dry nitrogen for approximately 15 minutes. The reactor was charged with 0.5035 g cyclohexanol. 1.2037 g *N,N*-diethyl-1,1,2,3,3,3-hexa-fluoropropylamine was added via a high pressure addition tube under nitrogen atmosphere. The whole reaction system was closed and *N,N*-diethyl-1,1,2,3,3,3-hexa-fluoropropylamine was flushed into the 25 mL reactor by using high pressure carbon dioxide. The reaction mixture was stirred at 25°C and at 1000±15 psi (6.9 ± 0.1 mPa) for 24 hours. The resultant solution mixture was analyzed by ¹H NMR and GC/MS.

Example 3

A 25 mL high pressure reactor equipped with a pressure transducer and temperature controller was purged by dry nitrogen for approximately 15 minutes. The reactor was then charged with 0.6373 g benzyl alcohol. 1.4287 g *N,N*-diethyl-1,1,2,3,3,3-hexa-fluoropropylamine was added to a high pressure addition tube under nitrogen atmosphere. The whole reaction system was closed and *N,N*-diethyl-1,1,2,3,3,3-hexa-fluoropropylamine was flushed into the 25 mL reactor by using high pressure carbon dioxide. The reaction mixture was stirred at 25°C and at 1000±15 psi (6.9 ± 0.1 mPa) for 20 hours. The resultant solution mixture was analyzed by ¹H NMR and GC/MS. The desired fluorinated product, alpha-fluorotoluene, was obtained in 60 percent yield.

Example 4

A 25 mL high pressure reactor equipped with a pressure transducer and temperature controller was purged with dry nitrogen for approximately 15 minutes. The reactor was then charged with 0.5721 g 1-octanol. 1.103 g *N*,*N*-diethyl-1,1,2,3,3,3-hexa-fluoropropylamine was added to a high pressure addition tube under nitrogen atmosphere. The whole reaction system was closed and *N*,*N*-diethyl-1,1,2,3,3,3-hexa-fluoropropylamine was flushed into the 25 mL reactor by using high pressure carbon dioxide. The reaction mixture was stirred at 25°C and at 1000±15 psi (6.9 ± 0.1 mPa) for 20 hours. The resultant solution mixture was analyzed by ^1H NMR and GC/MS. The desired fluorinated product, 1-fluorooctane, was obtained in 68 percent yield.

Example 5

A 25 mL high pressure reactor equipped with a pressure transducer and temperature controller was purged with dry nitrogen for approximately 15 minutes. The reactor was then charged with 0.5745 g 2-octanol. 1.12 g *N*,*N*-diethyl-1,1,2,3,3,3-hexa-fluoropropylamine was added to a high pressure addition tube under nitrogen atmosphere. The whole reaction system was closed and *N*,*N*-diethyl-1,1,2,3,3,3-hexa-fluoropropylamine was flushed into the 25 mL reactor by using high pressure carbon dioxide. The reaction mixture was stirred at 25°C and at 1000±15 psi (6.9 ± 0.1 mPa) for 20 hours. The resultant solution mixture was analyzed by ^1H NMR and GC/MS. The desired fluorinated product, 2-fluorooctane, was obtained in 48 percent yield.

Example 6

A 25 mL high pressure reactor equipped with a pressure transducer and temperature controller was purged by dry nitrogen for approximately 15 minutes. The reactor was then charged with 0.1585 g cholesterol. 1.2689 g *N*,*N*-diethyl-1,1,2,3,3,3-hexa-fluoropropylamine was added to a high pressure addition tube under nitrogen atmosphere. The whole reaction system was closed and *N*,*N*-diethyl-1,1,2,3,3,3-hexa-fluoropropylamine was flushed into the 25 mL reactor by using high pressure carbon dioxide. The reaction mixtures was stirred at 25°C and at 1000±15 psi (6.9 ± 0.1 mPa) for 20 hours.

The resultant solution mixture was analyzed by ^1H NMR and GC/MS. The desired fluorinated product, cholesteryl fluoride, was obtained in 62 percent yield.

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Example 7

A 25 mL high pressure reactor equipped with a pressure transducer and temperature controller was purged with dry nitrogen for approximately 15 minutes. The reactor was then charged with 0.0971 g cholesterol. 1.349 g *N,N*-diethyl-1,1,2,3,3,3-hexa-fluoropropylamine was added to a high pressure addition tube under nitrogen atmosphere. The whole reaction system was closed and *N,N*-diethyl-1,1,2,3,3,3-hexa-fluoropropylamine was flushed into the 25 mL reactor by using high pressure carbon dioxide. The reaction mixtures were stirred at 0°C and at 1000±15 psi (6.9 ± 0.1 mPa) for 20 hours. The resultant solution mixture was analyzed by ^1H NMR and GC/MS. The desired fluorinated product, cholesteryl fluoride, was obtained in 28 percent yield.

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Example 8

A 25 mL high pressure reactor equipped with a pressure transducer and temperature controller was purged with dry nitrogen for approximately 15 minutes. The reactor was then charged with 0.1033 g cholesterol. 1.2634 g *N,N*-diethyl-1,1,2,3,3,3-hexa-fluoropropylamine was added to a high pressure addition tube under nitrogen atmosphere. The whole reaction system was closed and *N,N*-diethyl-1,1,2,3,3,3-hexa-fluoropropylamine was flushed into the 25 mL reactor by using high pressure carbon dioxide. The reaction mixture was stirred at 25°C and at 1000±15 psi (6.9 ± 0.1 mPa) for 20 hours. The resultant solution mixture was analyzed by ^1H NMR and GC/MS. The desired fluorinated product, cholesteryl fluoride, was obtained in 33 percent yield.

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Example 9

A 25 mL high pressure reactor equipped with a pressure transducer and temperature controller was purged with dry nitrogen for approximately 15

minutes. The reactor was then charged with 0.1002 g cholesterol and 1.5042 g sodium fluoride. 1.2332 g *N,N*-diethyl-1,1,2,3,3,3-hexa-fluoropropylamine was added to a high pressure addition tube under nitrogen atmosphere. The whole reaction system was closed and *N,N*-diethyl-1,1,2,3,3,3-hexa-fluoropropyl amine was flushed into the 25 mL reactor by using high pressure carbon dioxide. The reaction mixture was stirred at 25°C and at 1000±15 psi (6.9 ± 0.1 mPa) for 20 hours. The resultant solution mixture was analyzed by ¹H NMR and GC/MS. The desired fluorinated product, cholesteryl fluoride, was obtained in 37 percent yield.

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Example 10

A 25 mL high pressure reactor equipped with a pressure transducer and temperature controller was purged by dry nitrogen for approximately 15 minutes. The reactor was then charged with 0.1018 g cholesterol. 1.1298 g *N,N*-diethyl-1,1,2,3,3,3-hexa-fluoropropylamine was added to a high pressure addition tube under nitrogen atmosphere. The whole reaction system was closed and *N,N*-diethyl-1,1,2,3,3,3-hexa-fluoropropylamine was flushed into the 25 mL reactor by using high pressure carbon dioxide. The reaction mixture was stirred at 40°C and at 1200±15 psi (8.3 ± 0.1 mPa) for 20 hours. The resultant solution mixture was analyzed by ¹H NMR and GC/MS. The desired fluorinated product, cholesteryl fluoride, was obtained in 51 percent yield.

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Example 11

A 25 mL high pressure reactor equipped with a pressure transducer and temperature controller was purged with dry nitrogen for approximately 15 minutes. The reactor was then charged with 0.1072 g cholesterol. 1.3062 g *N,N*-diethyl-1,1,2,3,3,3-hexa-fluoropropylamine was added to a high pressure addition tube under nitrogen atmosphere. The whole reaction system was closed and *N,N*-diethyl-1,1,2,3,3,3-hexa-fluoropropylamine was flushed into the 25 mL reactor by using high pressure carbon dioxide. The reaction mixture was stirred at 40°C and at 1500±15 psi (10.3 ± 0.1 mPa) for 20 hours. The resultant solution mixture was analyzed by ¹H NMR and

30

GC/MS. The desired fluorinated product, cholesteryl fluoride, was obtained in 45 percent yield.

Example 12

5 A 25 mL high pressure reactor equipped with a pressure transducer and temperature controller was purged with dry nitrogen for approximately 15 minutes. The reactor was then charged with 0.1056 g cholesterol. 1.1132 g *N,N*-diethyl-1,1,2,3,3,3-hexa-fluoropropylamine was added to a high pressure addition tube under nitrogen atmosphere. The whole reaction
10 system was closed and *N,N*-diethyl-1,1,2,3,3,3-hexa-fluoropropylamine was flushed into the 25 mL reactor by using high pressure carbon dioxide. The reaction mixture was stirred at 40°C and at 2000±15 psi (13.8 ± 0.1 mPa) for 20 hours. The resultant solution mixture was analyzed by ¹H NMR and GC/MS. The desired fluorinated product, cholesteryl fluoride, was obtained in
15 33 percent yield.

Example 13

 A 25 mL high pressure reactor equipped with a pressure transducer and temperature controller was purged with dry nitrogen for approximately 15
20 minutes. The reactor was then charged with 0.1054 g cholesterol. 1.2434 g *N,N*-diethyl-1,1,2,3,3,3-hexa-fluoropropylamine was added to a high pressure addition tube under nitrogen atmosphere. The whole reaction system was closed and *N,N*-diethyl-1,1,2,3,3,3-hexa-fluoropropylamine was flushed into the 25 mL reactor by using high pressure carbon dioxide. The
25 reaction mixture was stirred at 40°C and at 3000±15 psi (20.6 ± 0.1 mPa) for 20 hours. The resultant solution mixture was analyzed by ¹H NMR and GC/MS. The desired fluorinated product, cholesteryl fluoride, was obtained in 29 percent yield.

Example 14

30 A 25 mL high pressure reactor equipped with a pressure transducer and temperature controller was purged with dry nitrogen for approximately 15 minutes. The reactor was then charged with 0.1176 g cholesterol. 1.2090 g

N,N-diethyl-1,1,2,3,3,3-hexa-fluoropropylamine was added to a high pressure addition tube under nitrogen atmosphere. The whole reaction system was closed and *N,N*-diethyl-1,1,2,3,3,3-hexa-fluoropropylamine was flushed into the 25 mL reactor by using high pressure carbon dioxide. The reaction mixture was stirred at 40°C and at 4500±15 psi (3.1 ± 0.1 mPa) for 20 hours. The resultant solution mixture was analyzed by ¹H NMR and GC/MS. The desired fluorinated product, cholesteryl fluoride, was obtained in 26 percent yield.

10 Example 15

202.4 mg of high density polyethylene (HDPE) was placed in a 800 mL reactor and evacuated for at least 3 hours at ambient temperature. Approximately 16 psi (1.1 kPa) of pure fluorine was slowly introduced into the reactor and the reaction temperature was controlled in the range of 21 to 23°C. The reaction was carried out at about 21-23°C for 20 hours and then reactor was carefully vented and evacuated under vacuum for at least 4 hours. The fluorinated HDPE was then placed in a vacuum oven for another 20 hours and the weight of fluorinated HDPE was 206.2 mg. The weight increased 3.8 mg. The depth of fluorination of HDPE was 12 to 21 μm which was measured by scanning electron microscopy.

Example 16

200.3 mg of high density polyethylene (HDPE) was placed in a 800 mL reactor and evacuated for at least 3 hours at ambient temperature. Approximately 16 psi (110 kPa) of pure fluorine was slowly introduced into the reactor and the reaction temperature was controlled from 21 to 23°C. Then, carbon dioxide was slowly added to the reactor until the total pressure of the reaction system was about 850 psi (5.8 mPa). The reaction mixture was stirred at about 21-23°C for 20 hours and then reactor was carefully vented and evacuated for at least 4 hours. The fluorinated HDPE was then placed in a vacuum oven for another 20 hours and the weight of fluorinated HDPE was 209.3 mg. The weight increased 7.6 mg. The depth of fluorination of HDPE was 54 to 62 μm which was measured by scanning electron microscopy.

Example 17

202.6 mg of high density polyethylene (HDPE) was placed in a 800 mL reactor and evacuated for at least three hours at ambient temperature.

5 Approximately 16 psi (110 kPa) of pure fluorine was slowly introduced into the reactor and the reaction temperature was controlled from 21 to 23°C. Then, carbon dioxide was slowly added to the reactor until the total pressure of reaction system is about 1150 psi (7.9 mPa). The reaction mixture was stirred at about 34-45°C for 20 hours and then reactor was carefully vented and

10 evacuated for at least 4 hours. The fluorinated HDPE was then placed in a vacuum oven for another 20 hours and the weight of fluorinated HDPE was 213.5 mg. The weight increased 10.9 mg. The depth of fluorination of HDPE was 65 to 75 μm which was measured by scanning electron microscopy.

Example 18

203.0 mg of high density polyethylene (HDPE) was placed in a 800 mL reactor and evacuated for at least three hours at ambient temperature.

Approximately 16 psi (110 kPa) of pure fluorine was slowly introduced into the reactor and the reaction temperature was controlled from 21 to 23°C. The

20 reaction was carried out at a temperature from about 34-35°C for 20 hours and then the reactor was carefully vented and evacuated for at least four hours. The fluorinated HDPE was then placed in a vacuum oven for another 20 hours and the weight of the fluorinated HDPE was determined to be 207.5 mg. The weight increased 4.5 mg. The depth of fluorination of HDPE was 29

25 to 42 μm which was measured by scanning electron microscopy.

Example 19

192.2 mg of low density polyethylene (LDPE) was placed in a 800 mL reactor and evacuated for at least three hours at ambient temperature.

30 Approximate 16 psi (110 kPa) of pure fluorine was slowly introduced into the reactor and the reaction temperature was controlled between 21 to 23°C. The reaction was carried out between 34 and 35°C for 20 hours and then reactor

was carefully vented and evacuated for at least four hours. The fluorinated LDPE was then placed in a vacuum oven for another 20 hours. The weight of the resulting fluorinated LDPE was determined to be 196.1 mg. The weight increased 3.9 mg. The depth of fluorination of LDPE was 12 to 20 μm which
5 was measured by scanning electron microscopy.

Example 20

195.7 mg of low density polyethylene (LDPE) was placed in a 800 mL reactor and evacuated for at least 3 hours at ambient temperature.
10 Approximately 16 psi (110 kPa) of pure fluorine was slowly introduced into the reactor and the reaction temperature was controlled at 21-23°C. The reaction was carried out from about 20 to 23°C for 20 hours and then reactor was carefully vented and evacuated for at least four hours. The resulting fluorinated LDPE was then placed in a vacuum for at least four hours. The
15 fluorinated LDPE was then placed in a vacuum oven for another 20 hours and the weight of fluorinated HDPE was determined to be 199.8 mg. The weight increased 4.1 mg. The depth of fluorination of LDPE was 19 to 20 μm which was measured by scanning electron microscopy.

20

Example 21

195.8 mg of low density polyethylene (LDPE) was placed in a 800 mL reactor and evacuated for at least 3 hours at ambient temperature. Approximate 16 psi (110 kPa) of pure fluorine was slowly introduced into the reactor and the reaction temperature was controlled at 21-23°C. Then,
25 carbon dioxide was slowly added to the reactor until the total pressure of reaction system is about 850 psi (5.8 mPa). Reaction mixture was stirred at about 21-23°C for 20 hours and then reactor was carefully vented and evacuated for at least 4 hours. The fluorinated LDPE was then placed in a vacuum oven for another 20 hours and the weight of fluorinated LDPE was
30 203.1 mg. The weight increased 7.3 mg. The depth of fluorination of LDPE was 42 to 58 μm which was measured by scanning electron microscopy.

Example 22

195.0 mg of low density polyethylene (LDPE) was placed in a 800 mL reactor and evacuated for at least three hours at ambient temperature. Approximately 16 psi (110 kPa) of pure fluorine was slowly introduced into the reactor and the reaction temperature was controlled from about 21 to 23°C. Then, carbon dioxide was slowly added to the reactor until the total pressure of reaction system was about 1150 psi (7.9 mPa). The reaction mixture was stirred at about 34 to 45°C for 20 hours and then reactor was carefully vented and evacuated for at least four hours. The resulting fluorinated LDPE was then placed in a vacuum oven for another 20 hours and the weight of the fluorinated LDPE was 205.5 mg. The weight increased 10.5 mg. The depth of fluorination of HDPE was 42 to 65 μm which was measured by scanning electron microscopy.

In the drawings, specification, and examples there have been disclosed typical preferred embodiments of the invention and, although specific terms are employed, they are used in a generic and descriptive sense only and not for the purposes of limitation, the scope of the invention being set forth in the following claims.

THAT WHICH IS CLAIMED:

1. A method of fluorinating a substance, said method comprising:
 - providing a reaction mixture comprising a liquid or supercritical carbon dioxide reaction medium, a first reactant, and a second reactant, wherein said first reactant is a fluorinating reagent; and
 - contacting said first reactant and said second reactant in the carbon dioxide reaction medium such that said first reactant fluorinates said second reactant.
2. The method according to Claim 1, wherein said liquid or supercritical carbon dioxide is present at a pressure ranging from about 800 psia (5.5 mPa) to about 5000 psia (3.4 mPa).
3. The method according to Claim 1, wherein said first reactant is selected from the group consisting of elemental fluorine, a nucleophilic fluorinating agent, an electrophilic fluorinating agent, and mixtures thereof.
4. The method according to Claim 1, wherein said second reactant is selected from the group consisting of organic compounds, inorganic compounds, organic polymers, inorganic polymers, and mixtures thereof.
5. The method according to Claim 1, wherein said second reactant is a fluoropolymer suitable for melt processing.
6. The method according to Claim 5, wherein said fluoropolymer is a perfluoropolymer.

7. The method according to Claim 1, wherein said second reactant is a polymer in the form of a shaped article.

8. The method according to Claim 7, wherein said shaped article is
5 a vessel having an interior surface that is exposed to said first reactant.

9. The method according to Claim 1, further comprising the step of separating the fluorinated component from the reaction mixture.

10 10. The method according to Claim 1, wherein said second reactant has at least one active group, and wherein said step of contacting said first reactant and said second reactant comprises contacting said first reactant and said second reactant so that the fluorine present in said first reactant replaces
15 said at least one active group to fluorinate the second reactant and become covalently bonded to said second reactant in place of said at least one reactive group.

11. The method according to Claim 10, wherein the at least one active group is selected from the group consisting of hydrogen, hydroxyl,
20 carbonyl, halogen, and mixtures thereof.

12. The method according to Claim 1, wherein said second reactant has at least one unsaturated site, and wherein said step of contacting said first reactant and said second reactant comprises contacting said first reactant
25 and said second reactant so that said first reactant reacts with said second reactant at the unsaturated site such that said second reactant becomes fluorinated.

13. The method according to Claim 12, wherein the at least one
30 reactive site is an unsaturated bond, and wherein fluorine from the first reactant becomes covalently bonded to the second reactant at the at least one reactive site.

14. . . A method of fluorinating a substance, said method comprising:

providing a reaction mixture comprising a liquid or supercritical carbon dioxide reaction medium, a first reactant, and a pharmaceutical compound,

5 wherein said first reactant is a fluorinating reagent; and

contacting said first reactant and said pharmaceutical compound in the carbon dioxide reaction medium such that said first reactant fluorinates said pharmaceutical compound.

10 15. The method according to Claim 14, wherein said liquid or supercritical carbon dioxide is present at a pressure ranging from about 800 psia (5.5 mPa) to about 5000 psia (3.4 mPa).

15 16. The method according to Claim 14, wherein said first reactant is selected from the group consisting of elemental fluorine, a nucleophilic fluorinating agent, an electrophilic fluorinating agent, and mixtures thereof.

17. The method according to Claim 14, wherein said pharmaceutical compound is selected from the group consisting of sterols, carbohydrates, amino acids, peptides, nucleosides, antibiotics, anesthetics, and mixtures thereof.

18. The method according to Claim 14, further comprising the step of separating the fluorinated component from the reaction mixture.

25

19. The method according to Claim 14, wherein said pharmaceutical compound has at least one active group, and wherein said step of contacting said first reactant and said pharmaceutical compound comprises contacting said first reactant and said pharmaceutical compound so that the fluorine present in said first reactant replaces said at least one active group to fluorinate the pharmaceutical compound and become covalently bonded to said pharmaceutical compound in place of said at least one reactive group.

30

20. The method according to Claim 19, wherein the at least one active group is selected from the group consisting of hydrogen, hydroxyl, carbonyl, halogen, and mixtures thereof.

5

21. A reaction mixture comprising:

a first reactant;

a second reactant; and

a liquid or supercritical carbon dioxide reaction medium;

10

wherein said first reactant is a fluorinating reagent, and wherein said first reactant and said second reactant are present in said carbon dioxide reaction medium, said first reactant and said second reactant reacting in said carbon dioxide reaction medium such that said second reactant becomes fluorinated.

15

22. The mixture according to Claim 21, wherein the liquid or supercritical carbon dioxide is present at a pressure ranging from about 800 psia (5.5 mPa) to about 5000 psia (3.4 mPa).

20

23. The mixture according to Claim 21, wherein said first reactant is selected from the group consisting of elemental fluorine, nucleophilic fluorinating agents, electrophilic fluorinating agents, and mixtures thereof.

25

24. The mixture according to Claim 21, wherein said second reactant is selected from the group consisting of organic compounds, inorganic compounds, organic polymers, inorganic polymers, and mixtures thereof.

30

25. The method according to Claim 21, wherein said second reactant is a fluoropolymer suitable for melt processing.

26. The method according to Claim 25, wherein said fluoropolymer is a perfluoropolymer.

27. The method according to Claim 21, wherein said second reactant is a polymer in the form of a shaped article.

28. The method according to Claim 27, wherein said shaped article
5 is a vessel having an interior surface that is exposed to said first reactant.

29. The mixture according to Claim 21, wherein said second reactant comprises at least one unsaturated bond, and wherein said first reactant reacts with said second reactant at the unsaturated bond such that
10 the second reactant becomes fluorinated.

30. The mixture according to Claim 21, wherein said second reactant has at least one active group, and wherein said second reactant contacts said first reactant so that the fluorine present in said first reactant
15 replaces said at least one active group to fluorinate the second reactant.

31. The mixture according to Claim 30, wherein the at least one active group is selected from the group consisting of hydrogen, hydroxyl, carbonyl, halogen, and mixtures thereof.

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FIG. 1
SEM Photograph (600X) of Fluorinated HDPE

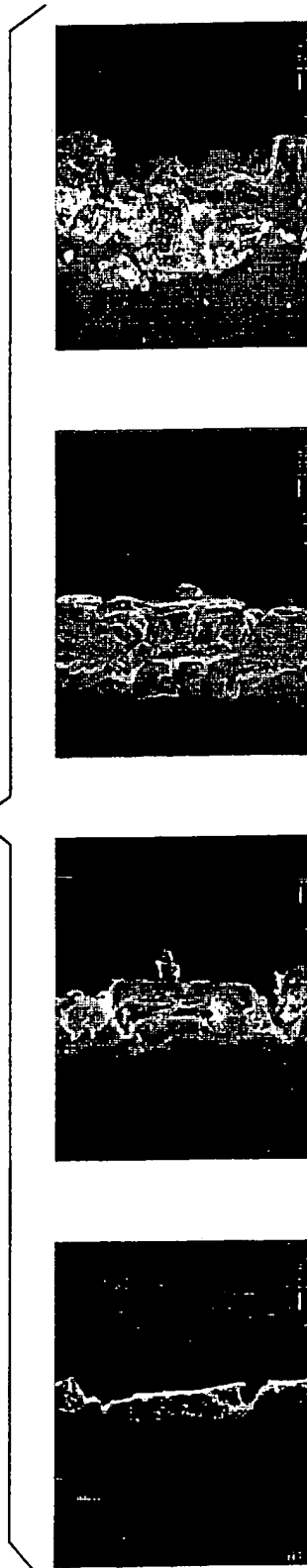
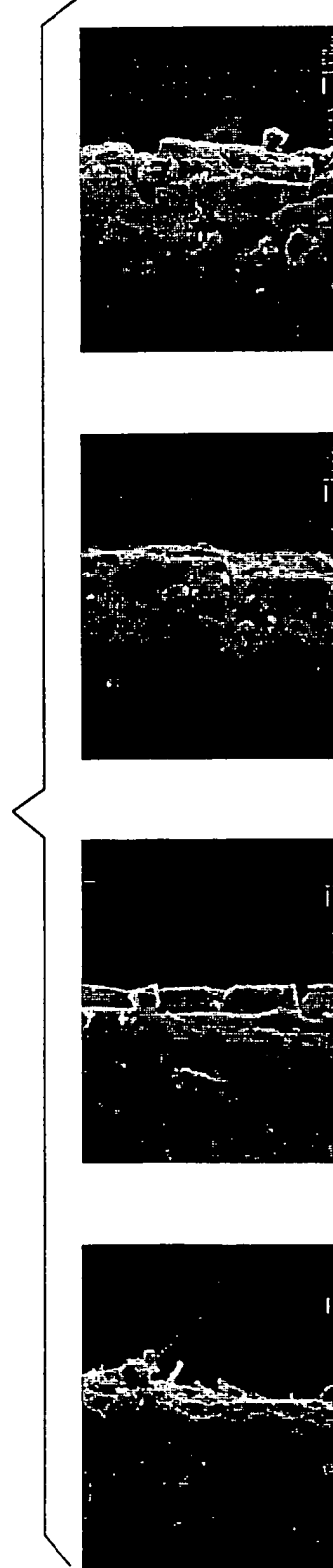


FIG. 2
SEM Photograph (600X) of Fluorinated LDPE



INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 00/11217

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C07B39/00 C07J9/00 C08F8/22 C08J7/12

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C07B C07J C08F C08J

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, PAJ, CHEM ABS Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	EP 0 489 197 A (LIQUID CARBONIC INC) 10 June 1992 (1992-06-10) the whole document ---	1-4, 21-24
P, X	DE 198 33 548 A (MESSER GRIESHEIM GMBH) 3 February 2000 (2000-02-03) the whole document -----	1-7, 21-27

☐ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents :

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Date of the actual completion of the international search

29 June 2000

Date of mailing of the international search report

06/07/2000

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INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US 00/11217

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
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